Use of antipsychotics in children and adolescents in the Spanish National Health System: network project with real-world data from five Autonomous Communities to inform evidence-based health policies (Children and Adolescents Antipsychotic Research for Evidence-based Strategies – CARES Project)

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000591

Study ID

1000000591

DARWIN EU® study

No

Study countries

Spain

Study description

The CARES project aims to support the development of public health policies and the rational use of antipsychotics (APs) in children and adolescents in Spain. It seeks to generate new, original, and relevant information on antipsychotic use patterns within the Spanish National Health System and analyse key aspects of the efficacy and safety of therapies used in the paediatric and adolescent population. The project will provide strategic intelligence for healthcare management and scientific insight into trends in AP use among young people, the characteristics of patients prescribed these drugs, their indications (including off-label uses), and their effects on young people's health. This information will allow for a detailed diagnosis of potential areas for public health intervention and rational drug use. To achieve this, the project will involve the four most populous autonomous communities in Spain (Andalusia, Catalonia, Madrid, and Valencia) as well as the Basque Country. Together, these regions represent 64% of the Spanish population, ensuring the project's findings are broadly representative.

Study status

Ongoing

Research institutions and networks

Institutions

Health Services Research and Pharmacoepidemiology Unit (HSRP Unit) FISABIO

Spain

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Institution | Other | ENCePP partner

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/04/2025

Actual: 01/04/2025

Study start date
Planned: 01/09/2024

Actual: 01/09/2024

Data analysis start date
Planned: 01/02/2025

Actual: 01/02/2025

Date of final study report
Planned: 31/12/2027

Sources of funding

- National competent authority (NCAs)

More details on funding

This study was funded by the Spanish Foundation for Science and Technology (FECYT), Ministry of Science, Innovation and Universities, grant FCT-24-20488, “Children and Adolescents Antipsychotic Research for Evidence-based Strategies – CARES project”.

Study protocol

12_Protocolo V001 [CARES].pdf (1023.71 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

A dynamic, population-based, retrospective cohort study comprising all individuals aged 0–19 years in the participating Autonomous Communities who

have initiated AP treatment (ATC N05A) between 1 January 2015 and 31 December 2023, with at least six months of follow-up.

Main study objective:

The general objective of this project is to inform the development of public health policies and rational use of APs in children and adolescents in Spain, generating new, original and relevant information on the use patterns of antipsychotic drugs in the SNS environment and analyzing the most relevant aspects of efficacy and safety of the therapies used in our child and adolescent population.

The project will generate strategic intelligence for management and at a scientific level on the trends in the use of AP in childhood and adolescence in our country, the characteristics of the patients to whom it is prescribed, the indications for which it is used, including all those unauthorized indications, and their effects on the health of our young people.

This information will allow obtaining a detailed diagnosis of potential areas of action in terms of public health and rational use of the medicine. To achieve this, the project will have the participation of the four Autonomous Communities with the largest population in the country (Andalusia, Catalonia, Community of Madrid and Valencian Community) as well as the Basque Country. In this way, we will have real-life data on 64% of the Spanish population, which will allow the results of the project to be broadly representative.

Specific objectives are:

First, to describe trends in the use of antipsychotics (AP) among patients aged 0 to 19 years (by Autonomous Communities and across all participating regions): temporal trends in the volume of prescriptions, number of patients treated with AP, and the evolution of prevalence and incidence rates of AP treatment. Trends will be described both overall and for specific APs of major interest (those with

the highest prescription levels: risperidone, aripiprazole, paliperidone, olanzapine, quetiapine, lurasidone, and other APs). All descriptive analyses will stratify data by variables of interest, such as age groups (0–4, 5–9, 10–14, 15–19), sex assigned at birth, family income level, and country of origin.

Second, to create a dynamic cohort (initially covering 2015–2023) of patients aged 0 to 19 years undergoing AP treatment in the participating Autonomous Communities. Multiple subcohorts (aggregated and by Autonomous Community) will be generated for initiators of the most frequently prescribed APs (risperidone, aripiprazole, paliperidone, olanzapine, quetiapine, lurasidone).
For each cohort, the following descriptive and analytical objectives will be pursued:

• To describe baseline sociodemographic and clinical characteristics of patients initiating AP treatment.

• To detail pharmacotherapeutic management patterns: prescribed indications, duration of treatment episodes, concomitant treatments (e.g., antidepressants, anxiolytics, antiepileptics), adherence indicators, and analysis of potential inadequacies based on the prescription indication. Stratified analyses will be performed for variables such as age groups, sex assigned at birth, family income, and country of origin.

• To describe the incidence of clinically relevant events in the cohorts of AP initiators.

• To assess the comparative safety of the main APs (olanzapine, risperidone, quetiapine, paliperidone, aripiprazole, lurasidone) for key prescribed indications and/or those identified as warranting special monitoring. Various potential adverse events will be evaluated, including neurological, motor, psychiatric, gastroenterological, metabolic, and cardiovascular events.

• To evaluate the comparative effectiveness of the main APs for key prescribed indications or identified priority indications, using appropriate operational

definitions for outcome measures derived from clinical history data in large databases (e.g., incidence of healthcare service contacts related to the condition for which the AP was prescribed, use of healthcare services, and concomitant medication use).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N05A) ANTIPSYCHOTICS

ANTIPSYCHOTICS

Population studied

Short description of the study population

Children and adolescents (0 to 19 years old)

Estimated number of subjects

1000000

Study design details

Setting

The study will be conducted among the population covered by the regional health systems of the participating Autonomous Communities, which provide healthcare to approximately 64% of the Spanish population, encompassing over four million individuals aged 0–19 years.

The cohort will include all patients who received an outpatient prescription or dispensing of an AP (ATC N05A) between 1 January 2015 and 31 December 2023 (or until the data extraction date). An incident treatment will be defined as a prescription for an AP in individuals with no prior prescription in the preceding six months. Individuals with limitations for long-term follow-up (e.g., not officially registered) and individuals without pharmaceutical coverage under the AVS, primarily those covered by public mutual societies (MUFACE, ISFAS, MUGEJU), due to limitations in identifying their pharmaceutical consumption in regional billing databases, will be excluded.

Data Sources Data will be obtained from the electronic clinical-administrative information systems of the participating regions. These systems integrate longitudinal sociodemographic and clinical data, enabling the construction of large population cohorts with rich and granular information at the individual patient level (diagnoses, treatments received, laboratory tests, hospital admissions, emergencies, and most healthcare interactions). This allows for the analysis of patient characteristics and treatment patterns and the evaluation of the cohorts’ exposure to different interventions, specifically the prescription of various APs for different indications.

Comparators

We will assess the comparative safety of the most prescribed APs in children and adolescents (olanzapine, risperidone, quetiapine, paliperidone, aripiprazole, lurasidone) for key prescribed indications and/or those identified as warranting special monitoring.

Outcomes

Number of AP prescriptions and treated patients per study year; Prevalence and incidence rates of AP treatments; Percentage of use for main indications of the most commonly prescribed Aps; Clinical outcomes for all patients and subcohorts, including: Hospitalisations and emergency visits for mental health-related conditions, Hospitalisations and emergency visits for myocardial infarction, cerebrovascular events, severe bacterial infections, and hip fractures, All-cause mortality during the follow-up period.

Data analysis plan

Initially, temporal trends in AP prescriptions and treated patients will be described, both overall and by AP type. Prevalence and incidence rates for AP treatment will also be estimated. Subsequently, initiator cohorts for APs in the participating regions will be constructed and characterised using baseline sociodemographic and clinical variables. Pharmacotherapeutic management patterns will be detailed, including prescribed indications, treatment duration, concomitant treatments, and potential inadequacies based on the prescription indication.

For key APs and main indications, comparative safety and effectiveness analyses will be performed. The incidence of clinical events of interest will be estimated for each comparator group, both crude and adjusted using propensity scores (PS). Multivariate logistic regression models will estimate PS, and intention-to-treat analyses will be the primary approach. Cox regression models will assess associations between APs and clinical events of interest, adjusted for baseline covariates and stabilised weights derived from PS. Hazard Ratios (HR) with 95% confidence intervals will be reported.

Secondary analyses will include per-protocol analyses, where follow-up will end with death, study completion, or treatment discontinuation. Sensitivity analyses will explore varying exposure periods, discontinuation definitions, and other

techniques to control for potential biases.

Summary results

The project will deliver novel insights into the patterns of AP use in children and adolescents, the main indications for their use, the characteristics of the patients who receive them, and health outcomes in terms of the safety and effectiveness of these drugs as used in routine clinical practice in Spain. This information represents an original and significant contribution to scientific knowledge, addressing a critical global lack of evidence regarding the use and effects of AP in young populations. Additionally, the findings will help identify healthcare policy priorities and guide the development of specific measures to improve the pharmacotherapeutic management of AP in children and adolescents in Spain.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

The Valencia Health System Integrated Database

The Information System for Research in Primary Care (SIDIAP)

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)

Data source(s), other

Osakidetzakoa (Basque country), Iraia (Andalusian region)

Data sources (types)

Biobank

Birth registry

Cancer registry

Congenital anomaly registry

Death registry

Drug prescriptions

Electronic healthcare records (EHR)

Laboratory tests and analyses

Pharmacy dispensing records

Population registry

Pregnancy registry

Vaccination registry

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after data extraction